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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/180,340	08/20/1999	NANCY W.Y. HO	7024109PUR48	6674

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EXAMINER

ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
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1653

no

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/180,340

Applicant(s)

Ho et al.

Examiner

HOPE ROBINSON

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jan 16, 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. PCT/US97/07663.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 19 6) ☐ Other:

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 6, 2003 has been entered.

2. Applicant's response to the Office Action mailed August 5, 2002 in Paper No.18 on January 6, 2003 is acknowledged. It is noted that applicant filed an Information Disclosure Statement on January 21, 2003 which has been considered.

Claim Disposition

3. Claims 14, 18, 25 and 28-30 have been amended. Claims 31-34 have been added. Claims 1-34 are pending.

4. The following grounds of rejection are or remain applicable :

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Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 13, 15, 16-17, 19-28, 30, 32 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 is indefinite because the claim recites “at least about 10 ribosomal DNA sites” and the range of “at least” is narrower than the range of “about” which goes outside of the first range. Therefore, the claim has a broad and narrow range and the specification does not provide any definition of the term “about”. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by “such as” and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required,

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or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

✓ Claim 25 is indefinite for the recitation of “substantially retaining its capacity for fermenting xylose to ethanol”, how much is considered to be “substantial retention” as the term is not defined in the specification (see also claims 22-23).

Claim 27 is indefinite because the claim does not clearly indicate that the claim is written for dependency upon claims 1, 22, 23, 24 etc. in the alternative or whether the claim simultaneously is dependent upon all listed claims. Where claim 27 depends from the listed claims, is it each one in the alternative or 1 and 22-25, or, 26 (for example, two different groupings of the claims).

✓ Claim 28 is indefinite for the recitation of “second section marker” instead of “second selection marker”.

Claim 30 is indefinite for the recitation of “a method for forming cells” as the method is describing a “method for producing progeny cells having multiple integrated copies of exogenous DNA”, not a method to *per se* “form cells”. The dependent claims are also included in this rejection.

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Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103 (a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

7. Claims 1-34 are rejected under 35 U.S.C. 103(a) as obvious over Ho et al. (WO95/13362, May 18, 1995) in view of Hallborn et al. (CA 2090122, October 17, 1991).

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Ho et al. teach recombinant yeasts containing genes encoding xylose reductase, xylitol dehydrogenase and xylulokinase, and DNA molecules, vectors and methods useful for producing such yeasts (see claim 1 of the instant invention). The recombinant yeasts effectively ferment xylose to ethanol, and preferred yeasts are capable of simultaneously fermenting glucose and xylose to ethanol (see claims 1 and 2 of the instant invention and the abstract and page 3 of the reference). The reference teach the fermentation of glucose to ethanol via the yeast *Saccharomyces* (see claim 3 of the instant invention and pages 3-5 of the reference). Ho et al. indicate that the yeast of the invention can ferment the two sugars (xylose and glucose) to ethanol simultaneously achieved where the xylitol dehydrogenase, xylulokinase and xylose reductase genes are fused to promoters which are not inhibited by the presence of glucose and also do not require xylose for induction (see page 6 of the reference and claims 5-8 of the instant invention). In addition, the recombinant yeast strain containing xylitol dehydrogenase, xylulokinase and xylose reductase genes are fused to non-glucose-inhibited promoters and the yeast is capable of fermenting xylose to ethanol and glucose to ethanol (see pages 6-7 and claim 9 of the instant invention).

Ho et al. teach direct amplification of the intact xylitol dehydrogenase gene and the promoter less xylitol dehydrogenase from *Pichia stipitis* chromosomal DNA (see Figure 10 and page 10). Furthermore, Ho et al. disclose that suitable sources of xylitol dehydrogenase, and xylose reductase genes include xylose-utilizing yeasts such as *Candida shehatae*, *Pichia stipitis*, *Pachysolen tannophilus* and suitable sources of xylulokinase genes include the above yeasts as

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well as xylose non-utilizing yeasts such as those from genus *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe* and bacteria such as *Escherichia coli* etc. (see page 13 and claims 10-12 of the instant invention). Additionally, the reference teaches selection markers in *S. cerevisiae* (see pages 15 and 16) and specific DNA fragments that serve as the replicon and selection markers that enable the plasmid to be replicated autonomously in *S. cerevisiae*. Further, it is disclosed that the yeast transformants containing the plasmid is distinguished from the untransformed host cells (see page 16). In-so-far-as Ho et al. do not explicitly teach the method as set forth in claim 14, Hallborn et al. teach recombinant yeasts that ferments xylose to ethanol, having genes integrated (multicopies) into the yeast chromosome. The genes taught by Hallborn et al. encode xylose reductase and xylitol dehydrogenase. Hallborn et al. also teach a yeast from *Saccharomyces* and a method of transforming cells with replicative and integrative plasmids (see pages 1-9 of the reference and claims 14-33 of the instant application).

Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole because Ho et al. and Hallborn et al. teach the fermentation of sugars to ethanol (i.e. xylose and glucose) using the same strain of yeast. One of skill in the art would reasonable expect successful results by combining the two references because Hallborn et al. teach an integrative plasmids and an autonomously replicating plasmid suitable for carrying out the transformation stably. Moreover, one of skill in the art would be motivated to combine the teachings of the references because Ho et al. disclose that ethanol is an ideal liquid fuel for

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automobiles and Hallborn et al. disclose a method to perform stable transformations over time.

Therefore, the claimed invention was *prima facie* obvious.

8. Claims 1-34 are rejected under 35 U.S.C. 103(a) as obvious over Ho et al. (WO95/13362, May 18, 1995) in view of Lopes et al. (Yeast, vol. 12, no.5, pages 467-477, April 1996).

Ho et al. teach recombinant yeasts containing genes encoding xylose reductase, xylitol dehydrogenase and xylulokinase, and DNA molecules, vectors and methods useful for producing such yeasts (see claim 1 of the instant invention). The recombinant yeasts effectively ferment xylose to ethanol, and preferred yeasts are capable of simultaneously fermenting glucose and xylose to ethanol (see claims 1 and 2 of the instant invention and the abstract and page 3 of the reference). The reference teach the fermentation of glucose to ethanol via the yeast *Saccharomyces* (see claim 3 of the instant invention and pages 3-5 of the reference). Ho et al. indicate that the yeast of the invention can ferment the two sugars (xylose and glucose) to ethanol simultaneously achieved where the xylitol dehydrogenase, xylulokinase and xylose reductase genes are fused to promoters which are not inhibited by the presence of glucose and also do not require xylose for induction (see page 6 of the reference and claims 5-8 of the instant invention). In addition, the recombinant yeast strain containing xylitol dehydrogenase, xylulokinase and xylose reductase genes are fused to non-glucose-inhibited promoters and the yeast is capable of

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fermenting xylose to ethanol and glucose to ethanol (see pages 6-7 and claim 9 of the instant invention).

Ho et al. teach direct amplification of the intact xylitol dehydrogenase gene and the promoter less xylitol dehydrogenase from *Pichia stipitis* chromosomal DNA (see Figure 10 and page 10). Furthermore, Ho et al. disclose that suitable sources of xylitol dehydrogenase, and xylose reductase genes include xylose-utilizing yeasts such as *Candida shehatae*, *Pichia stipitis*, *Pachysolen tannophilus* and suitable sources of xylulokinase genes include the above yeasts as well as xylose non-utilizing yeasts such as those from genus *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe* and bacteria such as *Escherichia coli* etc. (see page 13 and claims 10-12 of the instant invention). Additionally, the reference teaches selection markers in *S. cerevisiae* (see pages 15 and 16) and specific DNA fragments that serve as the replicon and selection markers that enable the plasmid to be replicated autonomously in *S. cerevisiae*. Further, it is disclosed that the yeast transformants containing the plasmid is distinguished from the untransformed host cells (see page 16). In-so-far-as Ho et al. do not explicitly teach integrative or replicative plasmids, Lopes et al. teach numerous plasmids containing various genes integrated into a ribosomal RNA gene of *Saccharomyces cerevisiae*. Multiple copies of the plasmid were successfully integrated into the genome (over 140 copies); which are stably maintained in non-selective medium for multiple generations over long periods of time (see abstract and pages 467-475). Further, the plasmids contained a Leu2d selection marker and various cloned genes for stability and expression studies. Yeast transformants were selected by

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plating on agar plates containing yeast nitrogen base (without amino acids), glucose and histidine. The same medium was used for growing the transformants in liquid culture (see page 468 and Figure 1 and see claims 14-33).

Therefore, It would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole by combining the teachings of Ho et al. and Lopes et al. because Ho et al. teach that the simultaneous fermentation of xylose and glucose into ethanol from the yeast *Saccharomyces cerevisiae*, as ethanol is said to be an ideal liquid fuel for automobiles and Lopes teach a method of making transformants stably maintained in non-selective medium for multiple generations over long periods of time. One of ordinary skill in the art would be motivated to combine the teachings of both references because the method taught by Ho et al. introduces DNA into the same yeast taught by Lopes et al. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

9. Applicant's arguments filed January 16, 2002 in Paper No. 18 has been considered. Note that the rejections of record have been withdrawn and new grounds of rejections have been instituted. Note that new grounds of rejections under 35 U.S.C. 103 have now been instituted applicant's comments in the response will be addressed as the references of record have been cited. Applicant contends that Ho et al. does not teach or suggest a "gene integrated at each of multiple reiterated ribosomal DNA sites". The response also contends that Ho et al. teach the introduction of plasmid constructs and that the examiner made an unjustified connection between

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introducing a plasmid and the subsequent integration of that plasmid. The response further contends that even if Ho et al. teach integration, they do not teach a yeast having genes integrated at each multiple reiterated ribosomal DNA sites of the yeast. This argument is not persuasive because the product as claimed is a yeast that ferments xylose to ethanol and the Ho et al. reference teaches the same yeast (*Saccharomyces*) and claim 1 is not directed to a method thus, the yeast of Ho would be expected to have the same properties of the claimed yeast as they are identical. The comments made in the response argue as though the claim is a product by processes claim and if so the Ho et al. reference is still relevant as the process is not important if the resulting product is the same. The MPEP states that "if the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process". The Ho et al. reference states that their method includes the step of introducing DNA into a yeast so as to cause the yeast to have introduced genes encoding xylose reductase etc. (see page 7), those although not explicit teaching, the suggestion was made which is the requirement under 35 U.S.C. 103. The process of integrative transformation includes the introduction of DNA into the yeast chromosome. In addition, integrative transformation of yeast is well known in the art. It is also not clear how the product of the Ho et al. reference differs from the product as claimed as the yeast of the reference ferments xylose to ethanol simultaneously with glucose as claimed. Thus, the reference anticipates the claimed invention. Note that the reference by Hallborn et al. has been cited to address the limitations in the method claims.

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Applicant's comments regarding the Le Dall et al. and Fujii et al. references have been considered, note that these references are not relied upon. Applicant contends that Lopes et al. do not teach autonomous replicating sequence. However, the reference teaches an integration system for *S. cerevisiae* which generates multiple copies (up to 200 integrated copies, thus, it is clear that the plasmid is able to replicate autonomously). In addition, the Lopes et al. reference is not to be analyzed on its own as the combined teaching of Ho et al. taken with Lopes et al. renders the claimed invention as obvious. Applicant states that claim 19 is a product by process claim and that the product of 19 is not the same as the prior art. Claim 19 recites a "yeast cells produced by the method of claim 18". Note that the method of claim 18 is disclosed by the references cited above and the references also teach the production of yeast cells. Thus, the claimed invention is obvious for the reasons stated above.

Art of Record

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Le Dall et al. (Current Genetics, vol. 26, pages 38-44, 1994). The reference provides multiple copies of plasmids that were successfully integrated into the genome yeast cells which expressed the Ura3 gene and could be maintained in non-selective medium for at least 20 generations.

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Fujii et al. (Applied and Environmental Microbiology, vol. 56, no. 4, pages 997-1003, April 1990). Fujii et al. teach an integration plasmid, pIARL28 containing the ribosomal DNA gene constructed for introduction of the α -acetolactate decarboxylase gene into brewer's yeast.

Conclusion

11. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The examiner can normally be reached on Monday and Wednesday-Friday from 9:00 am to 5:30 pm (EST).


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, can be reached at (703) 308-2923.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax your

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response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope Robinson, MS 

Patent Examiner



CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
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